UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

ASTELLAS INSTITUTE FOR REGENERATIVE MEDICINE, and STEM CELL & REGENERATIVE MEDICINE INTERNATIONAL, INC.,	)	
Plaintiffs,	)	C.A. NO. 1:17-cv-12239-DJC
v.	)	
IMSTEM BIOTECHNOLOGY, INC., XIAOFANG WANG, and REN-HE XU,	)	
Defendants.	)	

OPPOSITION TO PLAINTIFFS'
MOTION TO DISMISS IMSTEM AND XIAOFANG WANG'S COUNTERCLAIMS

TABLE OF CONTENTS

TABLE OF AUTHORITIES

Cases

Statutes

Defendants ImStem Biotechnology, Inc. and Xiaofang Wang hereby oppose plaintiff Astellas Institute for Regenerative Medicine ("Astellas") and Stem Cell & Regenerative Medicine International, Inc.'s ("SCRMI") (collectively, "plaintiffs") Motion to Dismiss the defendants' Counterclaim.

INTRODUCTION

This case is about whether the list of inventors on the face of U.S. Patent No. 8,961,956 (the "'956 patent") includes everyone who contributed to the invention in the patent. More precisely, the instant dispute concerns which scientists conceived of the idea of using hemangioblast-derived mesenchymal stem cells ("HB-MSC") to treat multiple sclerosis and other autoimmune diseases.

Dr. Wang contributed the central concept of the '956 patent. He should have been listed among the inventors when the '956 patent's application was filed. Yet the plaintiffs move to dismiss under Rule 12(b)(6) now, on no record, with no evidence, and before the Court has heard from a single witness. They have mischaracterized the relevant claims. They have contradicted their earlier statements to the Patent and Trademark Office ("PTO"). And perhaps most troubling, they have advanced an argument that – if taken seriously – would invalidate the very patent at issue. In their zeal to keep Dr. Wang off of the '956 patent they have attacked the core idea of the '956 patent itself. The Motion should be denied.

FACTUAL BACKGROUND

Mesenchymal stem cells ("MSCs") are quasi-differentiated cells that have the ability to become a wide range of bodily cells, such as bone, fat, and cartilage. While less pluripotent than human embryonic stem cells ("hESC"), they retain the ability to change and develop into a wide range of cell types.

In or about 2010 Drs. Kimbrel and Lanza developed a new kind of MSC derived from hemangioblasts ("hemangioblast-derived MSCs" or "HB-MSCs").[1] MSCs until that time had been derived from bone marrow, adipose tissues, umbilical cord blood, or directly from hESCs. Kimbrel and Lanza allegedly developed a new method of making MSCs comprising the steps of developing hESCs into embryoid bodies, then hemangioblasts, then HB-MSCs.

As the plaintiffs have admitted, they were not able to test their new cells *in vivo* at their joint-venture employer, SCRMI. Without fully understanding the cells they had, the plaintiffs approached Dr. Wang (through a mutual contact, Dr. Shi-Jiang Lu) to discuss testing the cells for MSC functionality. Countercl. (Dkt. 20) ¶¶ 18-20. In the course of those initial discussions, Dr. Wang suggested not only a way of testing the cells *in vivo* but specifically suggested the HB-MSCs could possibly be used to treat autoimmune diseases (his area of expertise). *Id.* ¶¶ 18-19. The resulting new method of using HB-MSCs to treat multiple sclerosis and other autoimmune diseases – conceived during that initial conversation of which Dr. Wang was very much a part – is the invention claimed in the '956 patent. Countercl. ¶¶ 32-34.

The early exchanges between Drs. Kimbrel and Wang are instructive. *See id.* ¶¶ 17-23. In her first email to Dr. Wang, Dr. Kimbrel wrote (referring to HB-MSCs) "I have not tested their functionality" and "I am not familiar with the EAE mouse model and am curious as to your thoughts on how you would use these cells in a model for autoimmune disease." *Id.* ¶ 20. Two weeks of emails followed. Then, on August 10, 2010, Dr. Wang obtained HB-MSCs from Dr. Kimbrel's lab. Compl. ¶ 35. He promptly started testing the functionality of HB-MSCs in the Experimental Autoimmune Encephalomyelitis ("EAE") mouse model. *Id.* ¶ 35. These

[1] ImStem and Dr. Wang assume, for purposes of the pending Motion only, that Kimbrel and Lanza invented the HB-MSCs themselves, an invention ultimately captured in U.S. Patent No. 8,962,321, not in suit.

experiments started yielding results in the early winter of 2010. *See* Countercl. ¶ 24. Before then, no one knew whether HB-MSCs could successfully treat *any* disease.

Drs. Kimbrel and Wang exchanged information about HB-MSCs through 2011. *See id.* ¶¶ 23-25. On November 30, 2011, Kimbrel and Lanza filed provisional patent Application No. 61/656,358 ("provisional application") – without informing or citing Dr. Wang. Countercl. ¶¶ 26, 35.[2] The application claimed HB-MSCs and their use to treat multiple sclerosis and other diseases. *Id.* ¶ 34; Ex. 1 (provisional application) at 49-50. The only data Kimbrel and Lanza cited on the functionality of HB-MSCs in treating any disease was the data they received from Dr. Wang.[3] *See* Countercl. ¶ 26.

On May 30, 2013, Kimbrel and Lanza filed Application No. 13/905,526 ("'526 application"), claiming priority to the provisional application. *See* Ex. 2 ('526 application); Ex. 3 ('956 patent) at 1 (citing both the provisional application and the '526 application).

On July 8, 2014, Wang and Kimbrel jointly published the results of their collaboration. Compl. ¶ 6. Their publication reported that HB-MSCs outperformed bone-marrow derived MSCs in mice with multiple sclerosis. *Id.*

On November 13, 2017, the plaintiffs filed suit against ImStem, Dr. Wang and Dr. Xu, seeking a correction of inventorship on a different patent.[4] On January 10, 2018, defendants

[2] The Exhibits to this Opposition are attached to the Declaration of Timothy R. Shannon in Support of Defendants' Opposition to the Plaintiffs' Motion to Dismiss ImStem and Xiaofang Wang's Counterclaims ("Shannon Decl.").

[3] Their patent application was not the only place Drs. Lanza and Kimbrel used Dr. Wang's work. In December of 2010, Dr. Kimbrel asked Dr. Wang for his testing data to present to a board meeting. Compl. ¶ 35. Dr. Wang obliged, giving Dr. Kimbrel the first ever test results proving the efficacy of HB-MSCs to treat any disease. *Id.* ¶ 35. Again on June 8, 2012, Dr. Lanza presented at the World Stem Cell Conference on, among other things, Drs. Xu and Wang's work.

[4] U.S. Patent No. 9,745,551.

counterclaimed on inventorship of the '956 patent. On January 31, 2018, the plaintiffs moved to dismiss.

LEGAL STANDARDS

Joint inventorship "is one of the muddiest concepts in the muddy metaphysics of the patent law." *Mueller Brass Co. v. Reading Industries, Inc.*, 352 F.Supp. 1357, 1372 (E.D. Pa. 1972). "Inventorship is a mixed question of law and fact: The overall inventorship determination is a question of law, but it is premised on underlying questions of fact." *Eli Lilly & Co. v. Aradigm Corp.*, 376 F.3d 1352, 1362 (Fed. Cir. 2004). "[T]he critical question for joint conception is who conceived, as that term is used in the patent law, the subject matter of the claims at issue." *Falana v. Kent State University*, 669 F.3d 1349, 1357 (Fed. Cir. 2012) (*citing Ethicon, Inc. v. U.S. Surgical Corp.*, 135 F.3d 1456, 1460 (Fed. Cir. 1998)).

When confronted with a motion to dismiss, "the court accepts as true all well-pleaded facts and draws all reasonable inferences in favor of the counterclaim plaintiff." *Metropolitan Property and Cas. Ins. Co. v. Boston Regional Physical Therapy, Inc.*, 538 F.Supp.2d 338, 341 (D. Mass. 2008) ("A motion to dismiss under Rule 12(b)(6) tests the sufficiency of the pleadings"); *see also Brandt v. Advanced Cell Tech. Inc.*, 349 F.Supp.2d 54, 57 (D. Mass. 2003) (denying dismissal); *United States v. Zajanckauskas*, 346 F.Supp.2d 251, 253 (D. Mass. 2003) (denying dismissal). Dismissal is only appropriate if the counterclaim, so viewed, fails to allege "a plausible entitlement to relief." *Rodriguez–Ortiz v. Margo Caribe, Inc.*, 490 F.3d 92, 95 (1st Cir.2007) (*quoting Bell Atl. Corp. v. Twombly*, 550 U.S. 544, 127 S.Ct. 1955, 1967 (2007)).

Dismissal of fact-dependent claims is especially disfavored. *McLaughlin v. Boston Harbor Cruise Lines, Inc.*, 419 F.3d 47 (1st Cir. 2005) (vacating 12(b)(6) dismissal and remanding for further findings partly because the "case is so fact-intensive"); *Kunelius v. Town*

of Stow, 2006 WL 1361226, at *1 (D. Mass. 2006) ("The remaining issues presented in the case, however, are fact-intensive, and it would be premature to dispose of them at this juncture.")

ARGUMENT

The Motion fails on four grounds. First, the plaintiffs have mischaracterized the relevant claims, confusing the *making* of HB-MSCs with the invention of *using* these HB-MSCs in a new way. Dr. Wang contributed significantly to the latter. Second, the plaintiffs' core argument is profoundly confused. If Dr. Wang's contribution was obvious, the claims themselves are obvious – and invalid under 35 U.S.C. § 103. Third, the Motion is premature; it presents many unresolved questions of material fact. Fourth, the plaintiffs' cases are inapposite.

A. The Plaintiffs Have Misstated the Invention Claimed in the '956 Patent

The central conception of the '956 patent is the idea of *using* HB-MSCs to treat multiple sclerosis and other autoimmune diseases. "[T]he claims of the '956 patent focus on methods of *using* [] novel MSCs to treat a disease or disorder." Mot. (Dkt. 22) at 5 (emphasis added). Claims 1 and 3 are illustrative:

> 1. A method for treating a disease or disorder, comprising administering to a subject in need thereof an effective amount of mesenchymal stromal cells or a preparation of mesenchymal stromal cells obtained by a method comprising culturing hemangioblasts under conditions that give rise to mesenchymal stromal cells.[5]
>
> 3. The method of claim 1, wherein the disease or disorder is selected from multiple sclerosis, systemic sclerosis, . . . psoriasis, or any combination thereof.

Ex. 3 ('956 patent) at 86:33-39, 86:43 87-6. Under Claim 3, whoever "administers . . . an effective amount" of HB-MSCs to treat an enumerated disease or disorder infringes the claim.

[5] Mesenchymal "stromal" cell is an alternative name for mesenchymal stem cells.

Put simply, the disputed claims are method claims, not composition-of-matter claims. 35 U.S.C. § 101 (distinguishing between "process" and "composition of matter" claims). They are not directed to the manufacture of the underlying HB-MSCs – the '956 patent's claims give no guidance as to how exactly the cells are made, only that they are HB-MSCs – but rather to their use once obtained. Put differently, the '956 patent does not claim the HB-MSCs themselves; it claims particular uses of the HB-MSCs once extant, *i.e.* what to do with them once you have them in hand.[6]

The named inventors conceded this point during prosecution. The '526 application originally contained over 100 claims, ranging from "mesenchymal cells hav[ing] replicative capacity to undergo at least 10 population doublings in cell culture with less than 25 percent of the cells undergoing cell death" (Claim 1) to "a method for generating mesenchymal stromal cells comprising culturing hemangioblasts." (Claim 46). Ex. 2 (original claims, as filed in '526 application) at 130-45. During prosecution, the PTO determined that the '526 application contained more than one invention and therefore issued a so-called "restriction requirement" compelling the applicants to pursue the two different inventions in two different patents. Ex. 4 (Examiner's restriction requirement) at 2. The PTO stated:

> Restriction to one of the following inventions is required under 35 U.S.C. § 121: I. Claims … drawn to mesenchymal stem cells and methods of making said cells. II. Claims … drawn to methods of treating diseases and disorders comprising administering mesenchymal stromal cells. . . . *Thus the inventions are patentably distinct.*

[6] A new use for an existing compound (or even a new compound) is patentable. By way of example, the original method patent for the erectile dysfunction drug, Viagra, claimed a novel use for a pre-existing compound. *See* U.S. Patent No. 6,469,012. The underlying compound had been known for years in treating heart disease and high blood pressure. *Id.* at 1:46-61. But as the inventors explained, "Unexpectedly, it has now been found that these disclosed compounds are useful in the treatment of erectile dysfunction," a different disorder and thus a patentably new use. The claims were directed to the use of the compound, not the compound itself. *Id.* That new use was patentable.

Id. at 2 (emphasis added). The claims concerning methods of treating autoimmune disease using HB-MSC cells were patentably distinct from the cells themselves and the method of making them. *Id.* They were different inventions.

At that point the plaintiffs could have argued that the inventions were not patentably distinct. They did not. Instead, in their reply, the plaintiffs merely stated:

> Applicant's representatives, the undersigned and Maria A. Trevisan [Applicant's legal counsel] conducted a telephone interview with the Examiner on October 1, 2014. Possible elections and claim amendments were discussed during the interview. The undersigned thanks the Examiner for the opportunity to discuss this Restriction Requirement. In response to the Restriction Requirement mailed May 29, 2014, Group II is elected for continued examination.

Ex. 5 (reply to restriction requirement) at 6. That is, Kimbrel and Lanza accepted the characterization, pursued the "methods of treating diseases [use]" claims, engaged in further patent prosecution, and eventually received the '956 patent.[7]

The instant Motion attempts to blur the distinction the PTO made (and the plaintiffs accepted) between cells and methods of making cells, on the one hand, and uses of the cells, on the other. The plaintiffs write, "The true inventors of the ['956 patent] developed a novel method of generating a specific type of stem cell . . ." Mot. at 1. Later they write, "Prior to the invention of the '956 patent, scientists derived MSCs directly from embryonic stem cells . . ." *Id*. at 2. These statements are misleading. As the plaintiffs admitted during prosecution, the '956 patent does not claim a method of "generating" HB-MSCs. Kimbrel and Lanza elected not to pursue such claims in the '956 patent. They instead pursued claims directed to what to do with such cells once obtained (*i.e*. therapeutic uses of them). The resulting patent claims a novel

[7] Kimbrel and Lanza made the opposite election in the prosecution of the sibling application (13/691,349) that ultimately issued as U.S. Patent 8,962,321. There, they pursued and claimed the method of making the cells and the cells themselves.

use for the cells – *i.e.* using them to treat *inter alia* multiple sclerosis – an idea supplied by Dr. Wang. The plaintiffs' characterization of the use of HB-MSCs to treat multiple sclerosis as "but a trifling component of the ['956 patent's] invention," is therefore beyond misleading. Mot. at 16. As they admitted during prosecution, use for treatment *is* the invention.

The plaintiffs are bound by that admission. Having knowingly acquiesced to the Examiner's characterization of the claims as being "drawn to methods of treating diseases and disorders comprising administering mesenchymal stromal cells", Ex. 4 (Examiner's restriction requirement) at 2, the plaintiffs are estopped from saying otherwise now. As the Federal Circuit has explained:

> Prosecution history estoppel . . . is not limited to the applicant's own words, but may embrace as well the applicant's responses to the examiner's actions. If the patentee does not rebut an examiner's comment or acquiesces to an examiner's request, the patentee's unambiguous acts or omissions can create an estoppel.

Glaxo Wellcome, Inc. v. Impax Laboratories, Inc., 356 F.3d 1348, 1357 (Fed. Cir. 2004).[8]

B. Dr. Wang's Contribution was Significant

The plaintiffs' admission during prosecution and again in their Motion – that the claims of the patent are directed to methods of use rather than the cells themselves – decides the Motion and the case. "It is a bedrock principle of patent law that the claims of a patent define the invention to which the patentee is entitled the right to exclude." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312 (Fed. Cir. 2005) ("That principle has been recognized since at least 1836, when Congress first required that the specification include a portion in which the inventor shall particularly specify and point out the part, improvement, or combination, which he claims as his own invention or discovery") (internal citations omitted). "We look to the words of the claims

[8] The plaintiffs admit it again in their brief, at one point admitting the "*claims* of the '956 patent focus on *methods of using* those novel MSCs." Mot. at 5 (emphasis added).

themselves . . . to define the scope of the patented invention." *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996). "The written description part of the specification itself does not delimit the right to exclude. That is the function and purpose of claims." *Markman v. Westview Instr., Inc.*, 52 F.3d 967, 980 (Fed. Cir. 1995). Put simply, this is a fight over inventorship of the *claimed* invention. The claims of the '956 patent are directed to treating certain diseases using these particular cells.

Dr. Wang contributed that very idea. Dr. Wang suggested to Kimbrel and Lanza that their collaboration focus on testing the effectiveness of these new HB-MSCs to treat autoimmune disease – his area of expertise. Countercl. at ¶ 18. Kimbrel and Lanza were not familiar with HB-MSCs' anti-inflammatory abilities or the cells' potential application in the area of autoimmune disease. *Id.* at ¶ 20. Thus, even if Kimbrel and Lanza supplied the underlying cells, it was Dr. Wang's idea to use them in the claimed way.[9]

Not only must the Court take these statements as true, the existing record supports them. The provisional application that gave rise to the '956 patent cited Dr. Wang's EAE model as the only support for treating any disease using HB-MSCs. Ex. 1 (provisional application) at 27. Further, the only exemplified disease was multiple sclerosis, Dr. Wang's area of expertise.

Moreover, even if Dr. Wang contributed one claim to the '956 patent, "[a] contribution to one claim is enough" to qualify a joint inventor. *Falana v. Kent State University*, 669 F.3d 1349, 1357 (Fed. Cir. 2012) (*citing Ethicon, Inc. v. U.S. Surgical Corp.*, 135 F.3d 1456, 1460 (Fed. Cir.1998). "All inventors, even those who contribute to only one claim or one aspect of one claim of a patent, must be listed on that patent." *Vapor Point LLC v. Moorhead*, 832 F.3d 1343,

[9] Furthermore, it was only his testing that confirmed that the HB-MSCs were true MSCs, with the functionality of MSCs.

1348–49 (Fed. Cir. 2016), *cert. denied sub nom. Nanovapor Fuels Grp., Inc. v. Vapor Point, LLC*, 137 S. Ct. 1121 (2017). *See also Fina Oil and Chemical Co. v. Ewen*, 123 F.3d 1466, 1473 (Fed. Cir. 1997) ("One need not alone conceive of the entire invention, for this would obviate the concept of joint inventorship."). The plaintiffs' suggestion to the contrary is wrong as a matter of law. Mot. at 16. Moreover, the '956 patent's multiple sclerosis claim is one of its most valuable features; the disease has no other known therapeutically effective treatment. Dr. Wang conceived of this claim, and should be rewarded for his contribution. *See Falana*, 669 F.3d at 1357.

C. The Plaintiffs' Core Argument is Self-Defeating

Rather than acknowledging the connection between the claimed invention (*i.e.* using HB-MSCs to treat *inter alia* multiple sclerosis) and Dr. Wang's contribution to that invention (*i.e.* the idea of using HB-MSCs to treat *inter alia* multiple sclerosis), the plaintiffs argue that Dr. Wang's entire contribution was "obvious." Mot. at 12. This argument is both wrong and deeply confused. If Dr. Wang's contribution was obvious, the claims themselves are obvious – and invalid under 35 U.S.C. § 103.

The plaintiffs' starting point is that it was "well known" that "MSCs could treat autoimmune diseases, including [multiple sclerosis]." Mot. at 9. According to the plaintiffs, "using MSCs to treat [multiple sclerosis] was in the prior art." *Id.* at 11. "There is nothing novel or inventive about the idea of . . . using MSCs to treat [multiple sclerosis]." *Id.* at 12. Setting aside whether Kimbrel and Lanza actually knew this allegedly-well-known concept (they did not), the plaintiffs are arguing that everyone in the art knew that MSCs could be used to treat multiple sclerosis, therefore everyone knew or would have known that HB-MSCs could be used to treat multiple sclerosis. *See, e.g.*, Mot. at 9-10. That, according to the plaintiffs, is why Dr. Wang's suggestion when he first met Kimbrel was "obvious." *Id.*

The entire argument is self-defeating. The uses identified in the '956 patent claims *are* the invention. Those enumerated, new, presumptively non-obvious therapeutic uses – never before claimed by anyone in any patent according to both the inventors and the PTO – are what distinguish the claimed inventions over the HB-MSC cells themselves. As noted above, these are method-of-use claims, not composition-of-matter claims. The identified and claimed uses are distinct from, *i.e.* not the same as, the underlying cells themselves. Hence the PTO's restriction order. Yet if, as the plaintiffs contend, those uses were already taught by (or obvious in light of) the prior art, the claimed uses would not be patentable. They would add nothing non-obvious to the cells themselves. The resulting claims would be obvious, and invalid. Put simply, if the claimed use was obvious, the method-of-use claim would be obvious and thus invalid. *Cf.* 35 U.S.C. § 103 (claims are not allowable if obvious over the prior art). The plaintiffs have doomed their own patent.

Their argument also creates other logical problems. For example, one assumption underlying their argument that "anybody would have guessed Wang's idea" is that using HB-MSCs must be the same as using prior art (non-HB) MSCs. Why else would papers and articles teaching the use of one kind of MSCs automatically teach/suggest/render obvious the use of another kind? Art that teaches the use of traditional MSCs to treat multiple sclerosis apparently teaches the use of HB-MSCs to treat multiple sclerosis. In short, MSCs are MSCs.

The plaintiffs come close to saying so explicitly. How else could they write:

> Dr. Wang contends he suggested to Kimbrel and Lanza that they evaluate whether their *hemangioblast-derived MSCs* could treat autoimmune diseases, including MS . . . . But that merely explains concepts well-known at the time— that *MSCs* might be useful to treat MS . . .

Mot. at 9 (emphasis added). These sentences only make sense if the reader assumes that HB-MSCs are the same as MSCs. Logically, Dr. Wang's idea of using HB-MSCs to treat multiple

sclerosis would add nothing to the art only if the art already taught using HB-MSCs. The art only taught using MSCs. The plaintiffs are arguing that MSCs and HB-MSCs must be the same.

Elsewhere the plaintiffs equate the prior art (concerning MSCs) with the claimed invention (concerning HB-MSCs). For example, the plaintiffs write that prior art concerning "MSC [and] autoimmune diseases and disorders," Mot. at 10 (*citing* '956 patent at 1:61-65) is "*identical* to what Dr. Wang purportedly contributed." *Id*. (emphasis added). "There is nothing novel or inventive about the idea of . . . using MSCs to treat [multiple sclerosis]." *Id.* at 12.

The entire argument is astonishing. The plaintiffs are erasing the distinction between prior art MSCs and HB-MSCs and, worse, arguing that the core concept of the '956 patent is obvious. Their argument all but invites this Court to invalidate the '956 patent on § 103 grounds. In their zeal to keep Dr. Wang off of the '956 patent by attacking his contribution (novel uses for HB-MSCs), the plaintiffs have attacked the core idea of the '956 patent itself (novel uses for HB-MSCs). Perhaps a sibling patent claiming the cells themselves could survive the plaintiffs' current argument, but the '956 patent is doomed.

The Court should reject the plaintiffs' unwittingly suicidal argument. The plaintiffs filed and obtained a patent on HB-MSCs by arguing they were not the same as prior art MSCs. *See* Ex. 3 ('956 patent) at 50: 5-11. ("In addition, experiments … compare different properties of ESC-MSCs or BM-MSCs versus hemangioblast- derived MSCs and reveal that these cells exhibit *significant differences* which may impact therapeutic efficacy of these cells and compositions derived therefrom.") (emphasis added).[10] The PTO agreed. Having knowingly acquiesced to the Examiner's determination that the use of HB-MSCs is non-obvious and patentably distinct from the HB-MSC cells themselves, the plaintiffs cannot tell this Court that

[10] *See also* Mot. at 2 (prior art MSCs were "of inconsistent quality and characteristics").

treating multiple sclerosis is simply obvious. They have already conceded that the use is non-obvious. *See Glaxo Wellcome*, 356 F.3d at 1357 (acquiescence to examiner's statements creates estoppel); *Phillips*, 415 F.3d at 1317 ("Like the specification, the prosecution history provides evidence of how the PTO and the inventor understood the patent."); *Alpex Computer Corp. v. Nintendo Co. Ltd.*, 102 F.3d 1214, 1220 (Fed. Cir. 1996) ("Prosecution history is relevant not only for purposes of prosecution history estoppel but also for construing the meaning and scope of the claims."). No one had used HB-MSCs to treat multiple sclerosis before the '956 patent's application was filed. The concept of such use was new. The concept was Dr. Wang's. *See* Countercl. ¶¶ 18- 20.[11]

The plaintiffs are not only barred from asserting Dr. Wang's contribution was obvious, the evidence of record suggests otherwise. If the notion of therapeutic use had been obvious, the plaintiffs could have (and would have) filed their patent application as soon as they had conceived of the HB-MSCs. To delay was to risk someone else patenting it first. That delay indicates the plaintiffs did not have the full concept until after working with Dr. Wang. Further, the '956 patent claims priority to the provisional ('358) application, filed on November 30, 2011. Thus the conception had to be complete by then, according to the plaintiffs. The '358 application contains a description of Dr. Wang's suggested and actual use, *see* Ex. 1 ¶¶ 056, 072, but does not cite any of the references cited in the '956 patent and the Motion to Dismiss. If such use was so well known, why did the plaintiffs not simply include these references in support of a prophetic example and file their application much earlier?[12] The answer is that they did not have the idea until they spoke with Dr. Wang.

[11] Furthermore, ImStem will present evidence that prior art teachings concerning MSCs and multiple sclerosis had suggested that MSCs might not be useful for treating multiple sclerosis. Many of the clinical trials had failed.

[12] As the plaintiffs, indeed, did for "Crohn's disease, ulcerative colitis, and the eye-disorder, oveitis." Ex. 1 (provisional application) at 29.

D. The Plaintiffs' Motion Raises and Relies Upon Many Disputed Fact Questions

Even if the foregoing were not enough to defeat the Motion (it is), the Motion itself is replete with fact questions that cannot be resolved at this stage of the proceeding. The case has only just begun, yet the Motion requires the Court to resolve fundamental and complex fact questions – on a technology the Court has not yet engaged.

The plaintiffs assert that Dr. Wang's suggested uses were well known in the art. Mot. at 9 n. 3 ("Dr. Wang did not introduce these concepts to the inventors"), 12 (similar). ImStem and Dr. Wang dispute this assertion. The scope and content of the prior art is well beyond the Court's ken at this stage of the proceeding. The interpretation of prior art is a matter of fact and expert discovery. This Court is ill-equipped to read highly technical articles about bio-molecular processes without the aid of an expert. Moreover, a self-serving specification itself characterizing the prior art, added by a patent lawyer to the non-provisional application a year after the provisional application, is an improper basis upon which to determine the scope and content of the prior art. Countercl. at ¶¶ 18-19 (Kimbrel and Lanza were not familiar with MSCs' potential use for autoimmune diseases; Dr. Wang suggested it).

The plaintiffs assert that studies teaching the therapeutic uses of MSCs are the same as teaching the therapeutic uses of HB-MSCs. Mot. at 9-10, 12. ImStem and Dr. Wang dispute this assertion. As important, the plaintiffs have admitted HB-MSCs were patentably new; the prior art therefore could not have taught their uses without rendering the entire patent invalid. *See supra; see also* Mot. at 9 (wavering on the point, saying it was known MSCs "might be" effective).

The plaintiffs assert that Kimbrel was aware of the potential uses of HB-MSCs and of the EAE model. Mot. at 9 n. 3. ImStem and Dr. Wang dispute this assertion. Countercl. ¶ 19. Dr.

Kimbrel wrote to Dr. Wang, "*I am not familiar with the EAE mouse model* and am curious as to your thoughts on how you would use these cells in a model for autoimmune disease." *Id*. at ¶ 20.

The plaintiffs assert that Kimbrel was a renowned authority on stem cells. ImStem and Dr. Wang dispute this assertion. Kimbrel knew nothing about the relevant EAE mouse model. She knew nothing about using HB-MSCs to treat multiple sclerosis. Countercl. ¶¶ 18-20.

The plaintiffs assert that the contribution of multiple sclerosis as one of the uses is "but a trifling component of the ['956 patent's] invention." Mot. at 16. ImStem and Dr. Wang dispute this. Multiple sclerosis is the most important valuable clinical application of this technology.

None of the relevant evidence is before the Court. Nor has the Court reviewed the prior art. Nor has the Court heard from a single witness. Nor has the Court seen a single document, email, or communication. Nor has the Court construed the claims. Nor has the Court heard from Dr. Lu, the head of research at Astellas' predecessor and the first point of contact with ImStem. There have been no document requests, no documents exchanged, no interrogatories, no depositions, no experts, no prior art.

Yet the plaintiffs would have this Court resolve questions of fact regarding the scope of the prior art, the scope of the claimed inventions, Dr. Kimbrel's knowledge before meeting Dr. Wang, the nature and scope of Dr. Wang's statements, and the scope and value of the resulting contribution to the '956 patent – all before a single piece of discovery has been exchanged.

The entire motion is wholly premature. It can and should be denied on that ground.

E. The Plaintiffs' Case Law is Inapposite

Finally, the plaintiffs' case law is inapposite. The plaintiffs attempt to analogize this case to *Burroughs Wellcome Co. v. Barr Labs, Inc.*, 40 F.3d 1223 (Fed. Cir. 1994). *See* Mot. at 13-15. In *Burroughs Wellcome*, the inventors were designing and synthesizing compounds for the express purpose of treating HIV. 40 F.3d at 1225-27. They already had proof of concept for the

success of these compounds in a mouse model. *Id.* at 1230-31. They had prepared a draft patent application for treatment of HIV, which the court found to be an enabling disclosure for human treatment. *Id*. at 1230. Thus, it was only after both conception and reduction to practice that the named inventors took their blinded samples to the NIH for testing in a human cell culture system, a system of which they were very much aware. *Id.* at 1230-31. The trial court unsurprisingly found the post-conception testing was not enough to give rise to a claim of co-inventorship. *Id*. at 1231.

In contrast, there is no evidence of record that Kimbrel and Lanza had any plans to treat multiple sclerosis when they developed their method for making HB-MSCs. There is no evidence that they had any plans to treat multiple sclerosis when they met Dr. Wang. The only evidence of record is to the contrary, *i.e.* before contacting Dr. Wang on July 29, 2010, Dr. Kimbrel did not know anything about the EAE mouse model for testing the autoimmune applications of HB-MSCs. Unlike the scientists at NIH in *Burroughs Wellcome*, Dr. Wang was not just confirming a proof of concept for an already-fully-formed idea. *See* 40 F.3d at 1225-27, 1230-31. He both gave Kimbrel the idea for treating multiple sclerosis and the means to reduce it to practice.

CONCLUSION

The plaintiffs' Motion is premature, confused, misleading, and self-sabotaging. The plaintiffs misread the '956 patent. They cite inapplicable caselaw. Their factual claims are contradicted by assertions in Dr. Wang's Counterclaims. They argue the core idea of the patent at issue was obvious – never mind that only nonobvious ideas are patentable. The Court should deny the Motion.

Dated: March 16, 2018

Respectfully submitted,

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CERTIFICATE OF SERVICE

I hereby certify that this document filed through the CM/ECF system will be sent electronically to the registered participants as identified on the NEF and paper copies will be sent to those indicated as nonregistered participants on March 16, 2018.

Dated: March 16, 2018

/s/ *Timothy R. Shannon*
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